REMARKS

On behalf of the Applicants, the undersigned wishes to express appreciation to Examiner Sharareh and his supervisor, Dr. Russell Travers, for the telephonic interview granted on October 7, 2003. This interview was extremely helpful in agreeing on claim language that would address the concerns of the Examiner and his Supervisor, as well as the Applicants.

Claims 2-26, 34, 36-38, 68 and 69 will remain in the application, after entry of this amendment.

Claims 1, 35 and 39-67 are being canceled, without prejudice, by this amendment.

New Claim 68 replaces Claim 1 and new Claim 69 replaces Claim 35.

New Claim 68 is the claim suggested by Examiner Sharareh to replace Claim 1 to overcome some 35 USC 112, second paragraph, concerns that he and his Supervisor had. This claim, with a few minor revisions to correct typos, is acceptable to Applicants. New Claim 68 recites all of the limitations of canceled Claim 1 but in a different format. It has been agreed that the limitation of Claim 1 obviated the rejections under 35 USC 102(b) as being anticipated by either U.S. Patent 4 844 907 (Elger et al) or U.S. Patent 6 238 695 (Makooi-Morehead et al). Hence, new Claim 68 obviates the 35 USC 102(b) rejection also.

In the note that accompanied the suggested generic claim, the Examiner noted that "the language and argument regarding the new claim must overcome the 103 rejection as well". However, the undersigned was unaware that the 35 USC 103 rejection was still an issue because it was not discussed during the telephonic interview on October 7, 2003 and has been discussed during the telephonic interview between the Examiner, the undersigned and the Applicants on May 1, 2003. The rejection is also addressed in the paragraph bridging pages 20 and 21 of Applicants' Response of July 8, 2003.

Nevertheless, the response to the 35 USC 103 rejection will be amplified below.

The claims are patentable over the combination of references applied because the combination of references does not establish a prima facie case of obviousness.

The establishment of a prima facie case of obviousness requires (1) some suggestion or motivation to modify or combine references, (2) a reasonable expectation of success and (3) that the combination of references teach or suggest all the claim limitations. The combination of references applied by the Examiner does not provide evidence that meets the criteria of a prima facie case for the following reasons:

U.S. PATENT 4 844 907 (Elger et al)
IN VIEW OF U.S. PATENT 6 238 695 (Makooi-Morehead et al)

The tablet composition of claim 1 requires the presence of

a) a rapidly precititating drug as the sole active pharmaceutical ingredient in an amount of about 5 to about 60%;

b) a polymeric binder in an amount of about 2 to about 60%;

c) a superdisintegrant in an amount of about 6 to about 40%; and

d) a lubricant in an amount up to about 5%.

The Elger et al patent describes a tablet that requires the presence of two active pharmaceutical ingredients, namely a narcotic analgesic and a non-steroidal anti-inflammatory. Elger et al also specifically teaches that they exclude lubricants such as "stearic acid/stearate salts from their tablets (especially magnesium stearate). See column 3, lines 33-35.

Makooi-Morehead et al disclose a compressed tablet or capsule comprising efavirenz, and one or more disintegrants that enhance the the dissolution rate of efavirenz in the gastrointestinal tract. The tablet requires the presence of a

lubricant, see item (f) in the list of ingredients in column 5, lines 40-50. Also, efavirenz is not in a salt form.

Motivation for combining references cannot be found where the proposed modification would render the prior art unsatisfactory for its intended purpose. MPEP § 2142, *In re Gordon*, 221 USPQ 1125 (Fed. Cir. 1984).

Since Elger et al specifically excluded lubricants of the type required by Makooi-Morehead et al from their tablets, the use of Makooi-Morehead et al to modify the Elger et al tablet would result in the rendering of Elger et al unsatisfactory for its intended purpose. In this regard, the Examiner's attention is directed to Elger et al, column 5, lines 5 through column 7, line 15 where Comparative Examples A through C are described. In each of the Examples, tablets that contained lubricants exhibited various problems such as poor crushing strength, sticking problems on compression, unacceptable disintegration rates and discoloring. The claimed tablets contain a lubricant; however, by using Applicants' specific combination of ingredients, none of the problems disclosed by Elger et al are experienced with Applicants' tablet composition.

CLORPRES® PACKAGE INSERT
IN VIEW OF U.S. PATENT 6 238 695 (Makooi-Morehead et al)

CLORPRES® is a combination of clonidine hydrochloride and chlorthalidone (a diuretic) that produces a more pronounced antihypertensive response than occurs after either clonidine hydrochloride or chlorthalidine alone. The inactive ingredients of CLORPRES® tablets are:

ammonium chloride
colloidal silicon dioxide
croscarmellose sodium (Type A)
magnesium stearate
microcrystalline cellulose
sodium lauryl sulfate and

D&C yellow #10

None of these ingredients are polymeric binders, a required ingredient of the claimed tablet composition. Also, the relative amounts of the various ingredients are not disclosed in the CLORPRES® package insert.

There is no motivation to combine the CLORPRES® and Makooi-Morehead et al references because there is nothing in either reference that teaches or suggests such combination. The reason that the Examiner gives for combining the reference is that:

> "Nevertheless, it would have been obvious to one of ordinary skill in the art at the time of invention to employ lactose and colloidal silicone dioxide in suitable amounts within the compositions of Elger, or the formulation of Clorpres, and further optimize all concentrations in a tablet dosage form, because as taught by Makooi-Morehead, the ordinary artisan would have had a reasonable expectation of success in improving the rate of dissolution of a insoluble drug and subsequently its extent of absorption in GI track."

Makooi-Morehead et al does not either disclose or suggest that lactose and/or colloidal silicone dioxide improve the rate of dissolution. They specifically teach that the disintegrant or superdisintegrant is the ingredient that enhances the rate of dissolution of efavirenz (column 1, lines 14-20 and column 2, line 64 through column 3). There would be no motivation for one skilled in the art to add superdisintegrant to the Clorpres® tablet to enhance the dissolution rate of the active ingredients because the Clorpres® tablet already contains a superdisintegrant, namely croscarmellose sodium. Also, there would be no motivation to eliminate either one of the active ingredients since by doing so, the synergistic effect of the combination would be destroyed.

Even if combined, the Clorpres® package insert and Makooi-Morehead et al patent would still not establish a prima facie case of obviousness because neither reference discloses a tablet that contains a polymeric binder as that term is used

by Applicants. As pointed out above, none of the inactive ingredients contained in the Clorpres® tablet are polymeric binders. In making the rejection under 35 USC 103, the Examiner would modify the Clorpres® tablet by adding coloidal silicone dioxide and lactose to it. Colloidal silicone dioxide is considered by Makooi-Morehead et al to be a glidant and not a polymeric binder (see column 3, lines 29-32). Furthermore, colloidal silicone dioxide can be a separate ingredient in the claimed tablet composition, but it is not necessary to prepare the claimed tablet composition (see page 5 of Applicants' specification, lines 13-19). Finally, the Clorpres® tablet already contains colloidal silicone dioxide.

Lactose can also be a separate ingredient of the claimed tablet composition but its presence is also not absolutely necessary (see page 5, lines 5-12 of Applicants' specification). Since it optionally can be present as a separate ingredient in the claimed tablet composition, it would be clear to one skilled in the art that lactose is not included in Applicants' definition of a polymeric binder. The polymeric binder is a required ingredient of the claimed tablet composition.

In addition to not being a polymeric binder, as that term is used by the Applicants, lactose does not fit the generally accepted definition of a tablet binder, let alone a polymeric tablet binder. In the current common state of the art, lactose, which was disclosed by Makooi-Morehead et al, column 3, lines 22-23, to be a binder is more often considered to function primarily as a diluent, since it merely provides a limited degree of table bond. See The Merck Index, 11th (1989), paragraph 5221 and Handbook of Pharmaceutical Drug Excipients, Third Edition, page 276, copies of which are enclosed as Enclosures 1 and 2, respectively.

Since there is no motivation for combining the Clorpres® and Makooi-Morehead et al reference and their combination does not teach or suggest all of the limitations of claim 68, the

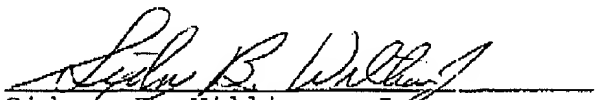
Examiner has not met the criteria for establishing a prima facie case of obviousness.

Specifically, the combination of the Clorpres® reference and Makooi-Morehead et al reference neither teach the use of a polymeric binder or the specific amounts of the ingredients recited in claim 1.

Since the dependent claims contain all of the limitations of claim 68, they are patentable over the combination of Elger et al and Makooi-Morehead et al and the combination of the Clorpres® reference for the same reason that claim 68 is patentable over the combination and because of the additional limitations contained in them.

In view of the above amendment and arguments, withdrawal of the rejections and expeditious passage of this application is respectfully solicited.

Respectfully submitted,



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Encl: The Merck Index, 11th Edition, 1989, page 843, paragraph 5221
Handbook of Pharmaceutical Drug Excipients, Third Edition, page 276
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